Journal of
Pulmonology and
Intensive Care

Case Report

DOI: 10.51271/JOPIC-0012

Pulmonary hypertension rapidly leading to mortality in a patient with interstitial pneumonia with autoimmune features

Esma Zenbilli, Kerem Ensarioğlu, Tuğçe Şahin Özdemirel, Berna Akıncı Özyürek

Department of Pulmonary Medicine, Ankara Ataturk Sanatoryum Training and Research Hospital, University of Health Sciences, Ankara, Turkey

Cite this article: Zenbilli E, Ensarioğlu K, Şahin Özdemirel T, Akıncı Özyürek B. Pulmonary hypertension rapidly leading to mortality in a patient with interstitial pneumonia with autoimmune features. *J Pulmonol Intens Care.* 2023;1(2):49-51.

Corresponding Author: Kerem Ensarioğlu, kerem.ensarioglu@gmail.com

Received: 03/03/2023 ◆ **Accepted**: 09/05/2023 ◆ **Published**: 22/05/2023

Abstract

Interstitial Pneumonia with Autoimmune Features (IPAF) is a newly defined connective tissue disease (CTD) related pulmonary involvement in 2015 by the European Respiratory Society and American Thoracic Society. It is used to define the subgroup of patients with no known CTD history. In this case report, we present a patient with IPAF diagnosis, who had rapid clinical deterioration after a COVID-19 infection, which was attributed to a newly diagnosed pulmonary hypertension. A 69-year-old male patient with chronic obstructive pulmonary disease (COPD) diagnosis was on the routine follow-up for a duration of five years. He had been diagnosed with type 2 diabetes mellitus and gout, with under constant follow-up for a known cardiovascular arterial disease history. During a routine pulmonary evaluation, the patient had stated a worsening exercise capacity and an increase in coughing. The requested high-resolution computed tomography showed emphysema at the upper lobes and a reticular pattern at the lower lobes, with honeycombing, traction bronchiectasis, and ground-glass findings. After a rheumatology consultation, which excluded the presence of an underlying rheumatological disease, the patient was diagnosed with IPAF. Under immunosuppressive treatment, the patient complained of increased dyspnea at a routine follow-up after a COVID infection in 2021, and antifibrotic treatment was initiated due to the progression of pulmonary fibrosis. During routine follow-up, further limitation in exercise capacity was evident, for which extra-pulmonary involvement was investigated. Pulmonary hypertension (PH) diagnosis was confirmed with vasoreactivity positivity; however, due to both progression in IPAF and concurrent PH, the patient was lost during the follow-up. As seen in this case, despite being stable for years, the addition of another comorbidity may rapidly worsen a patient's otherwise stable clinical condition. While antifibrotic regimens may be used on a case-by-case basis, their effect on disease progression may not be sufficient to control an already present comorbidity, such as pulmonary hypertension.

Keywords: Autoimmune, mortality, interstitial pneumonia, pulmonary hypertension

INTRODUCTION

Undifferentiated connective tissue diseases (UCTD) present with varying symptoms and different system involvement. The nomenclature comes from the diagnosis itself, as no specific underlying etiology is found in patients with UCTD. A sizeable group among these patients, up to 10-25%, are diagnosed with UCTD-related interstitial lung disease (ILD) at or during the follow-up. For those whose pulmonary involvement could not be classified under any known connective tissue diseases (CTD), the European Respiratory Society (ERS) and American Thoracic Society (ATS) defined Interstitial Pneumonia with Autoimmune Features (IPAF) description in 2015 (1).

IPAF remains a rare entity among UCTD, as it is a diagnosis of exclusion and requires evaluation of possible CTD (2). The diagnostic process is further complicated as IPAF may present itself with nonspecific radiological findings such as ground-class opacities and traction bronchiectasis (2-3). Additionaly, IPAF may be insidious in clinic setting as it can mimic clinical presentation of nonspecific interstitial pneumonia and has an overall better prognosis than idiopathic pulmonary fibrosis, which often leads to an indolent process that delays the diagnosis (3-4).

In this case report, we present a patient with an IPAF diagnosis who had rapid clinical deterioration after a COVID-19 infection, which was attributed to a newly diagnosed pulmonary hypertension.

CASE

A 69-year-old male patient with chronic obstructive pulmonary disease (COPD) diagnosis was on the routine follow-up for a duration of five years. He had been diagnosed with type 2 diabetes mellitus and gout, with under constant follow-up for a known cardiovascular arterial disease history. During a routine pulmonary evaluation, the patient had stated a worsening exercise capacity and an increase in

This work is licensed under a Creative Commons Attribution 4.0 International License.

coughing. In the physical examination, desaturation was present in room air at 80% with a finger probe and was consistent with the arterial blood gas sampling. Bilateral rales were heard in lung auscultation, with more prominent in the lower left zone. Clubbing was not evident, and there were no signs of cardiac failure.

The chest x-ray requested for initial evaluation showed a reticular pattern in the left lower zone and subpleural involvement in both lung zones. (**Figure 1**) For further investigation, high-resolution computed tomography (HRCT) was performed, which revealed emphysema at the upper lobes and a reticular pattern at the lower lobes, with honeycombing, traction bronchiectasis, and ground-glass findings present at the lower lobes. (**Figure 2**) In the connective tissue marker test panel, Scl-70 was found positive. A bronchoscopy was performed for the presence of additional pathologies, with bronchoalveolar lavage and transbronchial biopsy being non-diagnostic.

Figure 1. Chest X-ray performed at initial evaluation

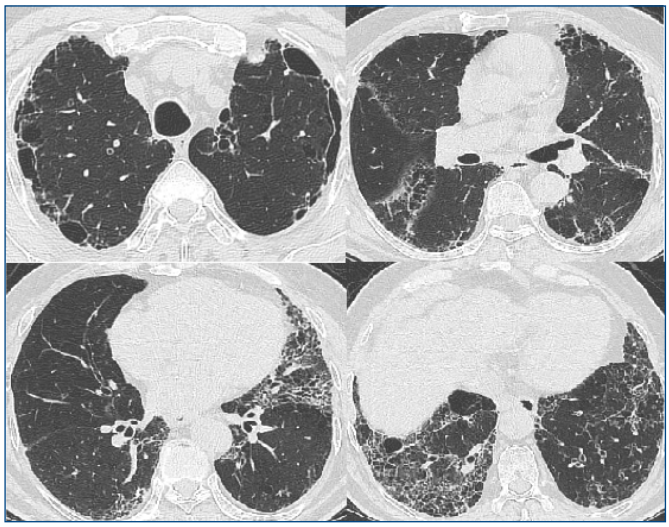

Figure 2. Tomography sections at initial evaluation

After a rheumatology consultation, which excluded the presence of an underlying rheumatological disease, the patient was diagnosed with IPAF. In a multidisciplinary council, the patient was put on an immunosuppressive regimen consisting of azathioprine and glucocorticoid. For a duration of 3 years, the patient was on the mentioned regimen, with a progressive decrease in drug dosage, and later, was on the follow-up with no treatment for two years as he was considered stable (**Figure 3**).

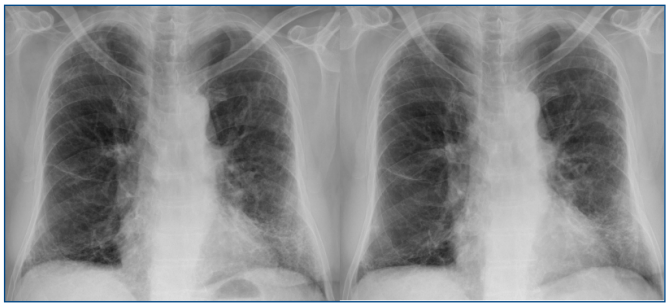

Figure 3. Chest X-ray follow-up 3 months and one year under treatment

At a routine follow-up after a COVID infection in 2021, the patient complained of an increase in dyspnea. In the requested HRCT, an increase in interstitial pattern, this time more predominant in the right lower lung, was observed (**Figure 4**). After consultation with the rheumatology department again for additional treatment requirement, the patient was evaluated once more at the multidisciplinary council, at which due to increased pulmonary fibrosis under immunosuppression, antifibrotic treatment was initiated as well nintedanib 150 mg twice daily.

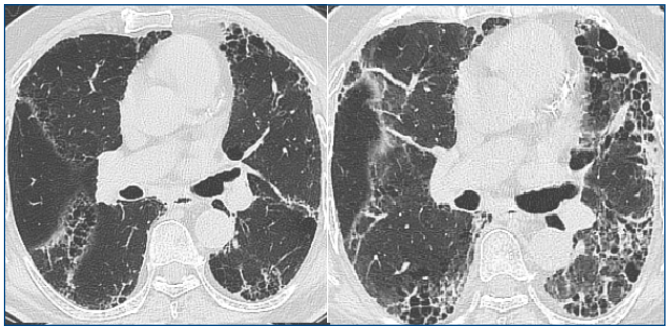

Figure 4. Tomography comparison performed at re-evaluation

During routine follow-up, further limitation in exercise capacity was evident, for which extra-pulmonary involvement was investigated. In echocardiography, an elevated systolic pulmonary arterial pressure (sPAB) of 50 mmHG was seen, and to evaluate pulmonary hypertension etiology, right heart catheterization was performed. Vasoreactivity was found positive, and the patient was put on a regimen of calcium channel blockers, for which limited response was seen. Due to respiratory failure attributed to IPAF and concurrent PHT, the patient was lost during the follow-up.

DISCUSSION

IPAF diagnosis requires four criteria; typical presentation in HRCT or a biopsy sample, exclusion of other etiologies, exclusion of known CTD and two criteria from a clinical and a serological list, which consists of CTD serological markers and clinical findings (2). Radiologically, IPAF may be presented with findings specific for non-specific interstitial pneumonia (NSIP), organizing pneumonia (OP) or combination of both, as well as lymphocytic interstitial pneumonia (LIP) (3). As NSIP is the most prevalent radiological pattern in IPAF at a 75.8%,

ground-class, reticular opacities and traction bronchiectasis are usually seen, with sparing of the subpleural areas (3). Compared to idiopathic pulmonary fibrosis (IPF), IPAF has a better prognosis, with a slow clinical deterioration (4).

IPAF treatment consists of immunosuppression as a sole agent or combined with a glucocorticoid regimen. In presence of respiratory failure, long term oxygen treatment is required for clinical control and symptomatic relief; and all patients eventually require pulmonary rehabilitation (4). Currently the justification for antifibrotic treatment is lacking due to insufficient data and studies are underway for their role in disease control (5).

Patient's Considerations

The patient, during the treatment duration, was compliant with the diagnosis and suggestions, however, expressed distress at the diagnosis of pulmonary hypertension. The informed consent for all treatment regimens and the presentation itself was received verbally and written from both the patient and the family.

CONCLUSION

As seen in this case, despite being stable for years, addition of another comorbidity may rapidly worse a patient's otherwise stable clinical condition. While antifibrotic regimens may be used as a case-by-case basis, their effect on disease progression may not be sufficient to control an already present comorbidity, such as pulmonary hypertension in this case. This limitation regarding comorbidities further stresses the point of routine evaluation and follow-up, as well as being vigilant for a possible change in treatment regimens when required.

ETHICAL DECLARATIONS

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Fischer A, Antoniou KM, Brown KK, et al. An official European Respiratory Society/American Thoracic Society research statement: interstitial pneumonia with autoimmune features. *Eur Respir J*. 2015;46(4):976-987. doi:10.1183/13993003.00150-2015
2. Graney BA, Fischer A. Interstitial Pneumonia with Autoimmune Features. *Ann Am Thorac Soc*. 2019;16(5):525-533. doi:10.1513/AnnalsATS.201808-565CME.
3. Yoo H, Hino T, Han J, et al. Connective tissue disease-related interstitial lung disease (CTD-ILD) and interstitial lung abnormality (ILA): Evolving concept of CT findings, pathology and management [retracted in: Eur J Radiol Open. 2022 Feb 11;9:100402]. *Eur J Radiol Open*. 2020;8:100311. doi:10.1016/j.ejro.2020.100311
4. Fernandes L, Nasser M, Ahmad K, Cottin V. Interstitial Pneumonia With Autoimmune Features (IPAF). *Front Med (Lausanne)*. 2019;6:209. doi:10.3389/fmed.2019.00209
5. Nagy A, Nagy T, Kolonics-Farkas AM, et al. Autoimmune Progressive Fibrosing Interstitial Lung Disease: Predictors of Fast Decline. *Front Pharmacol*. 2021;12:778649. doi:10.3389/fphar.2021.778649